Formulation and Evaluation of Orodispersible tablet of Montelukast sodium and Desloratadine

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ABSTRACT: ***The present study deals with the formulation and evaluation of orally disintegrating drug delivery system using Montelukast sodium along with Desloratadine for the treatment of allergic rhinitis, urticaria. The tablets were prepared using Direct compression technique using Pearlitol as filler, Sucralose as sweetner, Kyron T314 and Crospovidone XL10 as superdisintegrant. Optimization of Kyron T314 was done so as to achieve disintegration within 30 seconds. The formulated formulations were subjected to various evaluation parameters including wetting time, disintegration time, content uniformity and spectrophotometric simultaneous estimation. The in-vitro dissolution studies were performed by USP II type dissolution apparatus in 900 ml of 0.1N HCl medium for Desloratadine and 0.5%SLS for Montelukast sodium at 50 rpm and 37±0.5°C and was compared with the reference market formulation (Mondeslor).***

1. INTRODUCTION

Oral administration of drugs is the most preferred and convenient route because of ease of administration, self- medication, accurate dosage and patient compliance. Difficulty to swallow solid dosage form like capsules and tablets is a general problem for all age groups especially pediatric and geriatric patients mainly due to the physiological changes. Dysphagia (difficulty in swallowing) is associated with many medical conditions like Parkinson's disease, stroke, head and neck radiation therapy, AIDS, thyroidectomy and cerebral palsy. To improve patient compliance there is an urgent requirement to develop novel dosage form that can rapidly disintegrate or dissolve with saliva. Orodispersible tablets are beneficial for patients having dysphagia. There are certain fast dissolving dosage forms such as fast dissolving films, fast dissolving pellets and Orodispersible tablets. Fast dissolving drug delivery system is a type of dosage forms those dissolve/disintegrate/disperse in oral cavity without the aid of water. The drug employed in ODTs may be either hydrophobic or hydrophilic in nature but the excipients are always hydrophilic in nature. If the drug is hydrophobic the dosage form is called fast disintegrating tablets otherwise if drug is hydrophilic it is called Orodispersible tablets. These are also called mouth dissolving tablets, melt-in-mouth tablet, oro-dispersible, porous tablets, rapid disintegrating tablets, quick dissolving or orally disintegrating tablets [1,2].

The basic approach in the development of ODT is by the use of superdisintegrants such as sodium starch glycolate, crosscarmellose, poly-vinyl-pyrollidone, which provides disintegration of tablet after putting on tongue. The bioavailability of certain drugs may be increased due to the absorption of drug in oral cavity.

The CDER (Center for Drug Evaluation and Research), USFDA defines Orodispersible tablets (ODTs) as:

•A solid dosage form containing medicinal substances or active ingredients that disintegrates rapidly, usually within matter of seconds when placed on the tongue. A fast dissolving or disintegrating tablet may be defined as solid dosage forms that can dissolve or disintegrate within seconds in oral cavity forming a suspension or solution without administration of water.

•An orodispersible tablet may be defined as a solid dosage forms that can disintegrate into smaller granules which is dissolved in mouth slowly. Depending upon the formulation and size of tablet the disintegration time varies from few seconds to more than a minute [3].

To achieve the tablets fast dissolving properties:

- Water must quickly enter into the tablet matrix to cause rapid disintegration and instantaneous dissolution of the tablet.
- Incorporation of an appropriate disintegrating agent or highly water soluble excipients in the tablet formulation.

Recently several new advanced technologies have been employed for the formulation of orodispersible tablet such as Freeze-Drying Or Lyophilization, Tablet Molding, Spray Drying, Sublimation, Cotton Candy Process, Direct Compression etc[4, 5]. These techniques are based on the principle of increasing tablet porosity and/or addition of superdisintegrants and water soluble excipients. Allergy is a common problem among all age groups. Montelukast sodium is a leukotriene receptor antagonist used in the treatment of asthma and to relieve symptoms of seasonal allergies whereas Desloratadine works by binding to a receptor, known as the histamine H1 receptor, and blocking a biochemical called histamine from binding to this receptor. This prevents histamine from triggering a sequence of events that leads to things we commonly associate with hives and allergies in general, like itching, redness, and swelling. It is long acting tricyclic histamine antagonist with a selective H1 receptor histamine antagonist activity.

In the present study an attempt has been made to formulate the orodispersible tablet of Montelukast sodium and Desloratadine.

2. MATERIALS AND METHODS

Montelukast sodium and Desloratadine were obtained from Morepen laboratories, kyron T314 were obtained from corel pharma and all other materials talc, sodium stearyl fumarate, talc, sucralose etc used were of analytical grade.

Orodispersible tablet were prepared by direct compression technique. Montelukast sodium, desloratadine and other excipients (Table no.1) were sifted through sieve and were mixed thoroughly in a polybag. The mixture was then compressed using 9.8mm punch in 16 station compression machine (Cadmach).

Table No. 1 List of Formulations

Ingredients	F1	F2	F3	F4	F5	F6	F7
Montelukast sodium eq. to Montelukast	10.39	10.39	10.39	10.39	10.39	10.39	10.39
Desloratadine	5	5	5	5	5	5	5

Pearlitol	263.71	262.06	260.48	258.91	257.33	255.76	255.76
Kyron T314	1.5 (0.5%)	3.15 (1%)	4.73 (1.5%)	6.3 (2%)	7.88 (2.5%)	9.45 (3%)	-
Crospovidone XL 10	-	-	-	-	-	-	9.45 (3%)
Aspartame	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Aerosil-200	3	3	3	3	3	3	3
Sucralose	1	1	1	1	1	1	1
Bubble gum flavor	4	4	4	4	4	4	4
Banana flavor	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Talc	5	5	5	5	5	5	5
Sodium stearyl fumarate	6	6	6	6	6	6	6

3. PRECOMPRESSION PARAMETERS

3.1 Bulk density [6]

The term bulk density (ρ_b) refers to a measure used to describe a packing of particles. The bulk density of powder depends upon particle size distribution, particle shape and the tendency of the particles to adhere to each other. Bulk density can be determined by pouring blend into a graduated measuring cylinder using a funnel and weigh. The bulk density can be calculated using the formula-:

Bulk density = weight of powder (M) / bulk volume (V_b)

3.2 Tapped density [7]

Same measuring cylinder should be set for the determination of tapped density (ρ_t) that was used for the determination of bulk volume. The measuring cylinder containing a known mass of blend was tapped for a fixed (500) number of taps. The tapped density is calculated by the following formula-:

Tapped density (ρ_t) = weight of powder (M) / tapped volume (V_t)

3.3 Angle of repose (θ) [8]

It is an indication of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane. Angle of repose was determined using funnel method. The powder mixture is allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose is then calculated by measuring the height and radius of the heap of powder formed. It is calculated by the following formula-

$\tan \theta = h/r$

Where, θ = angle of repose, h =height in cm, r = radius in cm.

Angle of repose (degrees)	Flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

Table 2: Relationship between Angle of repose and flow properties

The lower the angle of repose, better the flow property. Rough and irregular surface of the particles gives higher angle of repose.

3.4 Carr's Index [9]

A simple way of measuring the free flow of powder. Carr's index measures the propensity of powder to be compressed and the flow ability of powder. Carr's index can be calculated from the bulk and tapped density by using following formula-

Carr's Index = (Tapped density (ρ_t) - Bulk density (ρ_b)) / Tapped density (ρ_t)

Consolidation Index (Carr %)	Flow
5-15	Excellent
12-16	Good
18-21	Fair to Passable
23-35	Poor
33-38	Very poor
>40	Very very poor

Table 3: Grading of the powders for their flow properties according to Carr's Index

3.5 Hausner's ratio

Hausner's ratio also measure the propensity and the flow ability of powder. Hausner's ratio can be calculated from the bulk and tapped density. Hausner ratio is given by the equation-:

Hausner's ratio= Tapped density (ρ_t) / Bulk density (ρ_b)

3.6 Fourier Transform Infra-Red (FTIR) Analysis:- Infrared spectrum of Montelukast Sodium and Desloratadine was determined by using Fourier transform infrared spectrophotometer using KBr dispersion method. The base line correction was done using dried Potassium Bromide. The spectrum of dried mixture of drug and KBr was used for analysis. The resulting spectra of Montelukast Sodium and Desloratadine are shown in Fig.8.2 and Fig. 8.4

4. EVALUATION OF ORODISPERSIBLE TABLET

The compressed tablet of Montelukast sodium and Desloratadine were evaluated for postcompression parameters.

4.1 Tablet weight variation

From each batch 20 tablets were randomly selected and their average weight was calculated. The individual weight of each tablet was compared with the average weight of 20 tablets. [10]

Percent of weight variation was calculated by given formula:

% of weight variation = [(Individual wt. – Average wt.)/ Average wt] × 100

Average weight of tablet	%Deviation
80mg or less	±10
More than 80mg but less than 250 mg	±7.5
250mg or more	±5

Table 4: Weight variation specification as per IP

4.2 Hardness

The hardness of the tablet was determined using Monsanto hardness tester. Tablet was placed between two anvils and force (kg/cm^2) was applied, the crushing strength that just caused the tablet to break was recorded. [11]

4.3 Tablet thickness and Diameter

The crown thickness and diameter of individual tablet was measured with a digital vernier caliper. Tablet thickness should be controlled within ±5% variation of the standard value of predetermined thickness. [12]

4.4 Friability

The friability of the tablet was measured using the laboratory friability apparatus, Roche friabilator. A pre weighed sample of tablets as placed in the friabilator and operated for 100 revolutions at 25rpm. The tablets were de-dusted, reweighed and %friability was calculated using following formula.

$F= [(W_{initial} - W_{final})*100]/ W_{initial}$

The accepted value for the tablets to pass friability is NMT 1% [13]

4.5 Wetting time

The WT of the tablets was evaluated. This experiment mimics the action of saliva in contact with the tablet. 5 tissue paper of diameter 10 cm were placed in a petri dish with 10cm diameter. A small volume of 10ml water containing ponceau 4R color was added to the petridish. The tablet was carefully placed on the filter paper at t=0 and the time for complete wetting was measured. The appearance of the color on the surface of the tablet was determined as the end point. [14-16]

4.6 In-vitro Disintegration Test

It is the time required by tablet to completely disintegrate. One tablet from each formulation was selected randomly and dropped in a 10 ml measuring cylinder containing 6 ml of distilled water. Time required by tablet to completely disintegrate was noted. Disintegration time depends on the quality and quantity of superdisintegrants used. It is measured in seconds. [17]

4.7 Drug Content Uniformity Test

Ten tablets were selected at random and average weight was calculated for both Montelukast sodium and Desloratadine. Tablets were crushed in a mortar and accurately weighed amount of drug was taken from the crushed blend. Then, the samples were transferred to 100ml volumetric flask and diluted up to the mark by methanol. The content was shaken periodically and kept for one hour to dissolve the drug completely. The mixtures were filtered and appropriate dilutions were prepared for both the drugs. The drug content in each tablet was estimated at λ_{max} against blank reference and reported. [18]

4.8 *In-Vitro* dissolution studies

In-Vitro drug release studies were carried out by using USP type II (paddle type) dissolution test apparatus at 50 rpm using 0.5%SLS and 0.1N HCL as dissolution media maintained at temperature of 37±0.5℃. samples were withdrawn at specific intervals and replaced with fresh media and filtered. The amount of drug dissolved was determined by spectrophotometrically at 345nm and 240 nm respectively. The experiments were conducted in triplicate. [19]

5. RESULTS AND DISCUSSION

5.1 FT - IR SPECTRA- Fourier Transform - Infra Red Spectroscopy of Montelukast sodium, Desloratadine, montelukast sodium and Desloratadine and of final optimized formulation was carried out and following graphs were obtained and are shown in fig 5.1, 5.2, 5.3 and 5.4

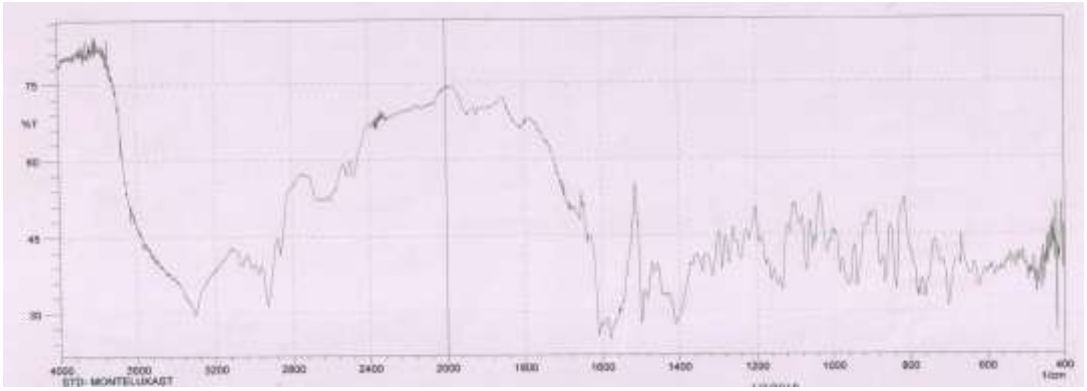

Fig 5.1: FTIR of Standard Montelukast sodium

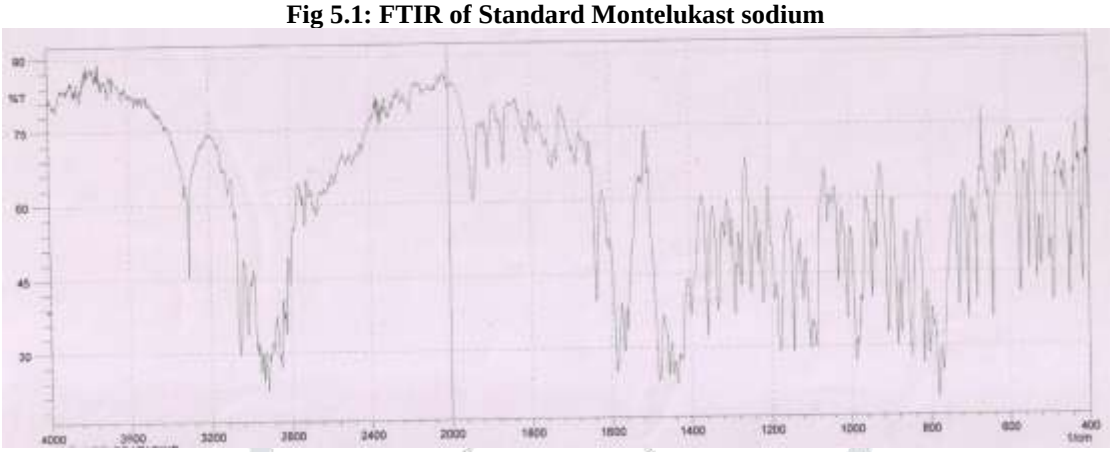

Fig 5.2: Graph of standard Desloratadine

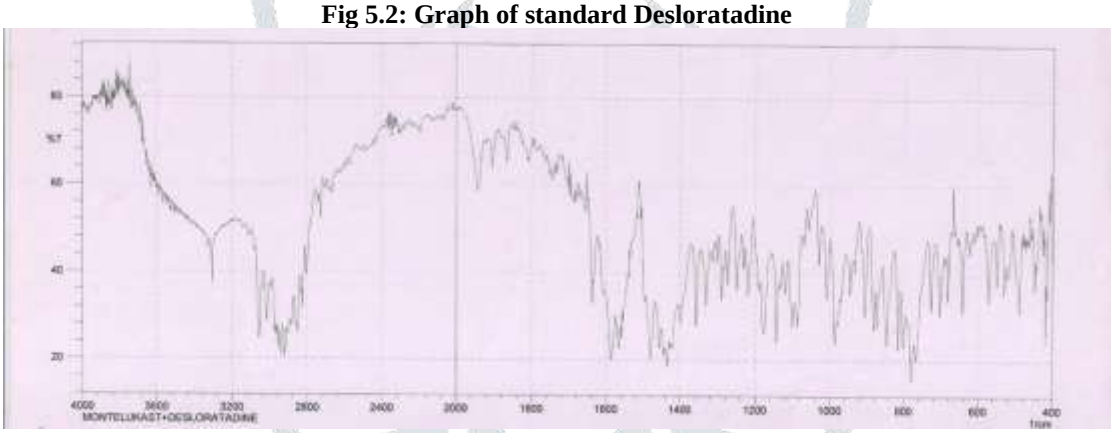

Fig 5.3 FTIR of Montelukast sodium and Desloratadine together

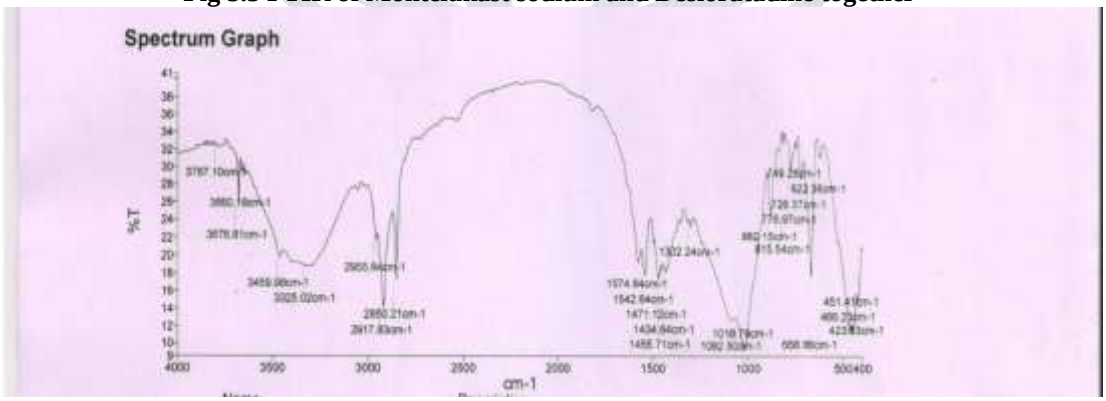

Fig 5.4: FTIR of Optimized formulation

5.2 PRECOMPRESSION PARAMETERS

Tablets were evaluated for its pre-compression parameters like Angle of Repose, Bulk Density, Tapped Density, Carr's Index, and Hausner Ratio. Observations are as follow: Angle of repose of all the formulations was found to be excellent ranging from 25.43 to 28.44. Formulation F2 showed lowest angle of repose i.e. 25.43, while formulation F1 showed highest angle of repose i.e. 28.44. Bulk density of all the formulations ranges from 0.54 gm/cm3 to 0.59 gm/cm3, while tapped density ranges from 0.65 gm/cm3 to 0.69 gm/cm3. Bulk density and tapped density of all the formulations were found to be limit

Carr's index of formulation F6 was found to be least i.e. 12.96 indicating that the powder had excellent compressibility and flow ability, while that of formulation F5 was found to be highest i.e. 16.81. Hausner ratio of all the formulations was found to be in limit i.e. less than 1.25 indicating that all the formulations had good flow ability of powder.

Trials	Bulk Density(gm/ml)	Tapped Density(gm/ml)	Angle of repose	Carr's Index	Haussner's Ratio
F1	0.57	0.68	28.44	15.83	1.12
F2	0.57	0.69	25.43	15.32	1.18
F3	0.56	0.66	27.65	15.10	1.21
F4	0.58	0.68	26.39	15.32	1.20
F5	0.54	0.65	27.69	16.81	1.19
F6	0.59	0.66	26.32	12.96	1.13
F7	0.59	0.69	27.69	14.01	1.19

Table 5: Precompression Parameters

5.3 POSTCOMPRESSION PARAMETERS

Tablets were evaluated for its post compression parameters like tablet thickness and diameter, hardness, friability, weight variation test, content uniformity test and in vitro release profile.

5.3.1 Thickness and Diameter:

Prepared tablets were observed for its thickness and diameter by using Vernier Caliper. Average thickness and diameter of each formulation observed is given in table 6

5.3.2 Hardness:

Hardness of prepared tablets were evaluated by Monsanto Hardness Tester. Mean of five tablets from each formulation was calculated and result is given in table 6

5.3.3 Friability:

Friability test was performed for all the formulations. 20 tablets or equivalent to 6.5gms from each formulation were weighed and placed in friabilitor to rotate for 100 times. Then tablets were then reweighed and percentage weight loss was calculated and result is given in table 6 . Friability of all the formulations was found to be in limit i.e. less than 1%. Friability of formulation F2 was found to be least while formulation F6 was found to be most friable amongst all formulations.

5.3.4 Weight Variation Test:

20 tablets from each formulation were weighed accurately and average weight of each formulation was calculated and result is given in table 6. All the formulations passed the weight variation test as each formulation showed less than 5% of deviation in weight.

5.3.5 Drug Content Uniformity Test:

Samples from each formulation were analyzed spectrophotometrically and obtained result is given in table 8 whereas for reference sample is shown in table 7

5.3.6 Wetting Time:

Wetting time of 3 tablets from each formulation was measured and mean was calculated to obtain the final result, which is given in table 8. Wetting time of formulation F6 was found to be least because of high amount of superdisintegrants in the formulation, while that of formulation F1 was found to be highest.

5.3.7 *In vitro* Disintegration Time:

Disintegration time of each formulation was measured and result is given in table 8. Disintegration time of formulation F1 was found to be maximum i.e. 85±2 seconds, while that of formulation F6 was found to be least i.e. 18 ± 3 seconds which is of course due to high amount of superdisintegrants used in the formulation. Formulation F7 showed slightly less disintegration time then the formulation F6 whereas reference conventional tablet (Mondeslor) manufactured by Sunpharma Pharmaceuticals showed disintegration time of 7 minutes shown in table 7

8.3.*8 In vitro* Release Profile:

- Samples were withdrawn at different intervals of 3, 6, 9, 12 and 15 minutes and diuted with 0.5%SLS. The samples were analyses at and 345 nm for Montelukast sodium using a UV/Visible double beam spectrophotometer. The results were computed in table 9 and fig 5.5
- Samples were withdrawn at different intervals of 3, 6, 9, 12 and 15 minutes and diuted with 0.1N HCL. The samples were analyses at 240 nm for Desloratadine using a UV/Visible double beam spectrophotometer. The results were computed in table 10 and fig 5.6
- Samples were withdrawn at different intervals of 5, 10, 15, 30, 45 minutes for market sample (Mondeslor) and diluted with 0.5%SLS. The samples were analysed at 345 nm for Montelukast sodium using a UV/Visible double beam spectrophotometer. The results were computed in table 11 and fig 5.7
- Samples were withdrawn at different intervals of 5, 10, 15, 30, 45 minutes for market sample (Mondeslor) and diuted with 0.1N HCL. The samples were analysed at 240 nm for Desloratadine using a UV/Visible double beam spectrophotometer. The results were computed in table 11 and fig 5.7

Formulation	Diameter (mm)	Thickness (mm)	% Friability	Weight variation (mg)	Hardness (kg/cm^2)
F1	9.8±0.01	3.8±0.1	0.47 ± 0.3	300±9.2	3.9±0.1
F2	9.6±0.02	3.9±0.2	0.47 ± 0.1	300±3.9	4.0±0.2

F3	9.8±0.02	3.9±0.1	0.48±0.2	299±1.5	3.8±0.1
F4	9.7±0.03	3.9±0.2	0.49±0.3	301±5.9	3.6±0.2
F5	9.8±0.01	3.9±0.2	0.48±0.4	301±7.7	3.8±0.2
F6	9.8±0.01	4.0±0.1	0.51±0.2	300±5.7	3.1±0.1
F7	9.8±0.01	3.8±0.1	0.50±0.1	300±8.0	3.5±01

Table 6: Observation of Diameter, Thickness, Hardness, %Friability and weight variation

Tests	**Marketed formulation (Mondeslor)**
Diameter (mm)	9.8±0.01
Thickness (mm)	3.8±0.2
Weight variation (mg)	301±6.5
Hardness (kg/cm$^{2)}$	3.9±0.1
Disintegration time (mins.)	**7**±1.0
% Drug content (Montelukast sodium)	98.10±1.7
% Drug content (Desloratadine)	99.80±0.8

Table 7: Observation of different parmeter of marketed formulation (Mondeslor)

Formulation	**Montelukast Sodium (% Drug quantity)**	**Desloratadine (% Drug Quantity)**	**Wetting time(sec.)**	**Disintegration time(sec.)**
F1	98.00±2.0	99.20±2.0	98 ± 2	85 ± 2
F2	98.10±1.9	99.80±0.9	83 ± 1	67 ± 1
F3	99.00±2.7	98.60±1.5	69 ± 1	45 ± 1
F4	98.60±2.3	99.20±2.0	53 ± 3	37 ± 2
F5	98.90±2.5	100.60±1.8	37 ± 2	29 ± 3
F6	100.30±2.0	99.60±1.2	21 ± 3	18 ± 3
F7	98.10±0.9	99.34±1.5	36 ± 2	27 ± 2

Table 8: % Drug Content, Wetting and Disintegration time of Different Formulations

Time (min.)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
0	0	0	0	0	0	0	0
3	43.08	43.62	38.79	55.99	54.45	56.91	51.25
6	49.88	53.89	49.57	66.79	63.09	63.09	61.16
9	60.40	63.75	65.27	73.60	72.36	68.68	72.48
12	70.36	73.63	75.46	80.72	80.71	81.01	80.55
15	81.28	83.82	83.35	87.23	88.45	92.14	90.68

Table 9: *In vitro* release of Montelukast sodium

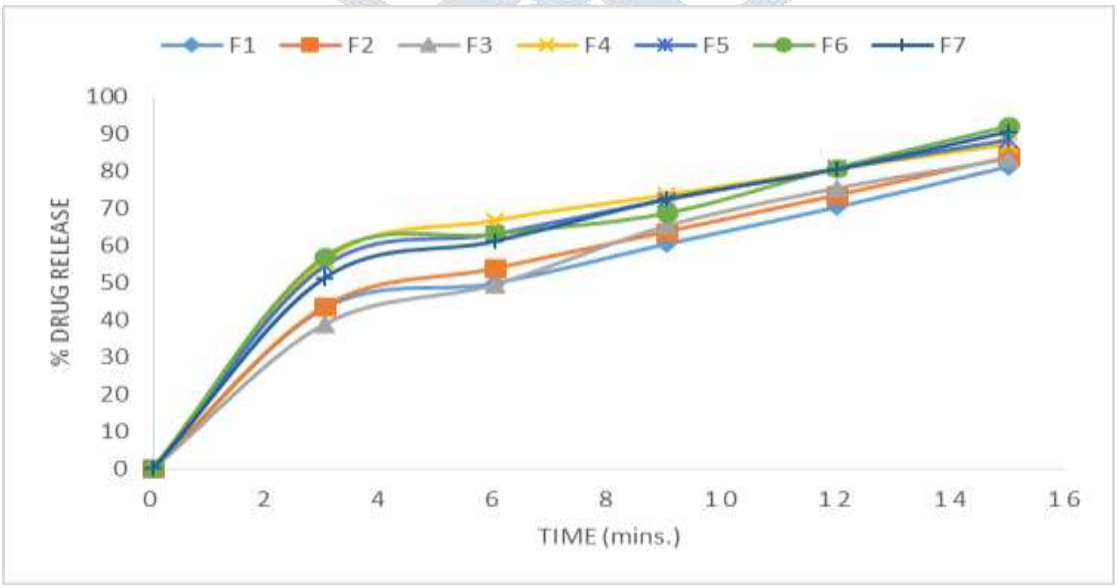

Fig 5.5: *in vitro* release profile of Montelukast sodium of all formulation

Time (min.)	F1	F2	F3	F4	F5	F6	F7
0	0	0	0	0	0	0	0
3	61.72	75.43	65.30	65.00	76.33	79.61	63.25
6	89.45	90.04	93.32	80.20	89.74	91.00	87.68
9	90.04	92.43	95.30	84.97	89.15	94.20	90.46
12	91.83	92.73	96.00	88.25	89.74	96.00	92.33
15	92.73	93.02	96.60	89.15	90.04	99.58	94.45

Table 10*: In vitro* release of Desloratadine

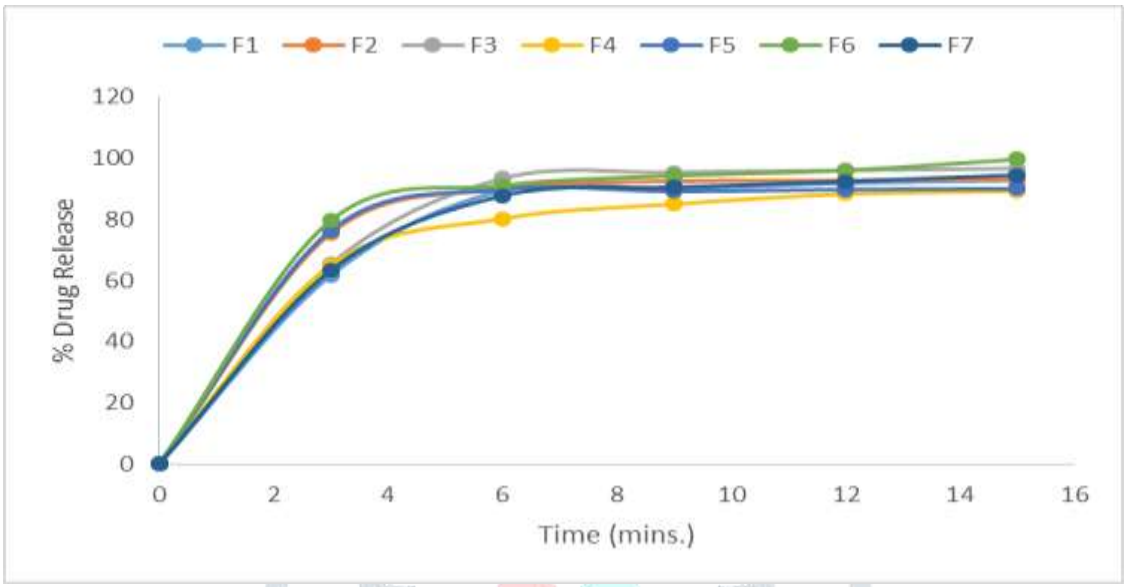

Fig 5.6: *in vitro* release profile of Desloratadine of all formulations

Time (mins)	Montelukast Sodium	Desloratadine
0	0	0
5	20.07	29.7
10	35.06	52.88
15	67.31	74.22
30	87.05	81.43
45	98.77	89.43

Table 11*: In vitro* release of Market sample (Mondeslor)

On comparison purpose, when compared with the optimized formulation (F6) Drug release was quite faster in comparison to market formulation. At the same time interval 15mins F6 formulation released 92.14% of montelukast sodium whereas market formulation released 67.31% of Montelukast sodium. Similarly the case , F6 formulation after 15 minutes released 99.58% of desloratadine in comparison to 74.22% release of desloratadine from the market formulation which indicates rapid dissolution of F6 formulation in comparison to the conventional market formulation (Mondeslor).

The relatively higher and faster release rate of drug from the developed ODT formulation as compared to the conventional marketed formulation.

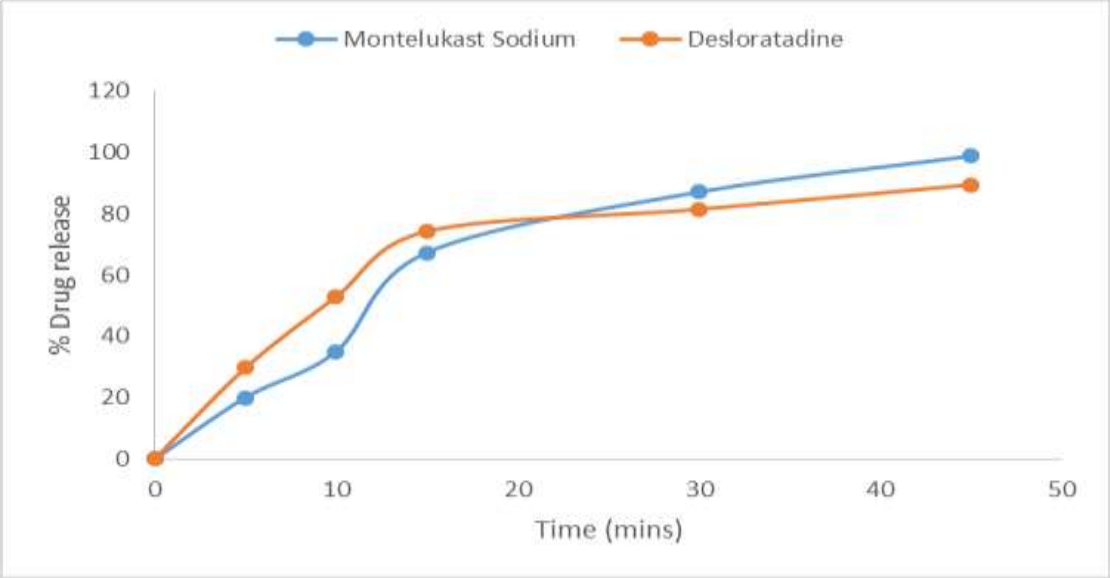

Fig 5.7 in vitro release of market formulation (Mondeslor)

.6. CONCLUSION

In the present study, Montelukast sodium and Desloratadine was selected to prepare orodispersible tablet. Purity and characterization of drug was done by FT-IR spectra within range from 4000 cm-1 to 400 cm. The solubility of the Desloratadine by oral conventional formulation are very low, so we successfully formulated the orodispersible tablets of Montelukast sodium and Desloratadine. Orodispersible tablet of Montelukast sodium and Desloratadine was effective and that it seemed to have less side effects. It may be an excellent drug for the urgent treatment of allergic rhinitis emergencies. Combination of superdisintegrants in different ratio were used to prepare the formulation by direct compression method. The superdisintegrants used was KyronT314. In the same concentration Crospovidone XL10 was used as to see which superdisintegrant had the better action. Other ingredients used were sodium stearyl fumarate, talc and pearlitol, aerosil and sucralose. The formulations were successfully prepared without any manufacturing defects. Powder blends of all formulations were evaluated and carr's index value was found to be satisfactory which suggested that the blends had good compressibility. Hausner ratio values obtained were also in limits ranging from 1.12 to 1.21

All the tablets maintained hardness in the range of 3.1- 4kg/cm^2 . The loss in total weight of the tablets due to friability was in the range of 0.18-0.6%. Friability of all the formulations was found to be in limit i.e. less than 1%. Formulation F6 which include Kyron T314 and Formulation F7 which included Crospovidone XL10 have a difference in disintegration and wetting time. Formulation F6 showed rapid disintegration when compared to Formulation F7. Formulation F6 was obtained as optimized formulation containing maximum amount of superdisintegrants, Kyron T314. As it showed a faster drug release in the dissolution profile and a rapid disintegration time.

The present research work revealed that the F6 showed better dissolution property than the conventional market formulation (Mondeslor) and better disintegration property then F7 containing superdisintegrant crospovidone XL10.

7. REFERENCE

[1] Kumar S, Gupta SK, Sharma PK. A review on recent trends in oral drug delivery-fast dissolving formulation technology. Advances in Biological Research. 2012;6(1):06-13.

[2] More S, Ghadge T. Fast disintegrating tablets: An overview. Asian Journal of Research in Pharmaceutical Science. 2013;3(2):47-55.

[3] Kumar S, Garg SK, Anseri A, Luhani P. Fast Dissolving Tablets (Fdts): Recent Trends And New Market Opportunities. Indo American Journal of Pharmaceutical Research. 2014; 4(07):3265-78.

[4] Sharma G. Mouth dissolving tablets: A current review o. system. 2013 Dec 30;9(10):11.

[5] VS. Ughde*, SV. Deshmane and KR. Biyani. A Review on Fast Dissolving Tablet- International Journal Of Pharmaceutical And Chemical Sciences. Jul-Sep 2015:4 (3).

[6] Hamilton EL, Luts EM. Advanced orally disintegrating tablets bring significant benefits to patients and product life cycle. Drug Deliv Technol. 2005; 5(1): 34-37.

[7] Chaudhuray J., Maity S., Sa B., Bandyopadhyay A.K., The East Pharm; 37: 121-3. (1994)

[8] Amrutha JV. Pre and Post Compression Studies of Tablets. An Indian Journal pg no- 1-2, July 28, 2016

[9] Biradar SS, Bhagvati ST, Kuppasad IJ. Fast dissolving drug delivery system:A overview. The Int. Journal Pharmacol. 2006; 4(2); 23-24.

[10] Lachman. L., Liberman. H., Kanig. J., third ed, The Theory and Practice of Industrial Pharmacy, Varghese Publication Bombay,296-306.(1990)

[11] Sanada H, Yonezawa Y and Danjo K: Preparation and evaluation of compressed tablet rapidly disintegrating in the oral cavity. Chem Pharm Bull. 1996; 44:2121-2127

[12] Lachman L and Lieberman HA. Pharmaeutical dosage forms of tablets. Vol II, Marcel Dekker (1981) 241-243

[13] Indian Pharmacopoeia. Government of India, Ministry of Health and Family Welfare, Published by the Controller of Publication, New Delhi. II, pp. 442. (2007)

[14] bandari S, Mittapalli RK, gannu R, Rao YM. Orodispersible tablets: an overview, Asian Journal of Pharma Times. 2008;40:11-15

[15] Remya K, Beena P, bijesh P, Sheeba A, Formulation and development, evaluation and comparative study of effects of super disintegrants in cefixime oral disintegrating tablets. J young Pharm 2010;2:234-9

[16] Rajpurohit H, Sharma P, Sharma S, Purohit S, Bhandari A, Hordeum vulgare hull in the design of fast disintegrating tablets, J Young pharm 2011;3:211-5

[17] Edmund J: Preparation, characterization and scale of ketoconazole with enhance the dissolution and bioavailability. Drug DevInd Pharm. 2007; 33:755-765.

[18] Indian Pharmacopoeia. Government of India, Ministry of Health and Family Welfare, Published by the Controller of Publication, New Delhi. II, pp. 663-665. (2007)

[19] Chowdhary KPR and Rao NR. Formulation and evaluation of dispersible tablets with pre gelatinised starch. Indian Drugs (1998) 35(6): 368-370.